Models of twin-twin transfusion syndrome

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Chapter 7

Does Amniotic Fluid Volume Affect Fetofetal Transfusion in Monochorionic Twin Pregnancies? Modelling Two Possible Mechanisms

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Abstract. Clinical evidence suggests that an increased amniotic fluid pressure due to polyhydramnios increases the placental vascular resistance. We sought to model the possible effects of an increased amniotic fluid pressure on the net fetofetal transfusion in monochorionic twin pregnancies. We wanted to compare these effects with results of previous simulations, which aimed to explain why twin-twin transfusion syndrome (TTTS) placentas include more often bidirectional arteriovenous (AV) than AV plus arterioarterial (AA) anastomoses. We extended our mathematical model of TTTS by simulating two different mechanisms that increases the placental vascular resistance as a consequence of polyhydramnios. First, an increase in the placental capillary resistance and hence in deep AV and opposite AV (denoted as VA) resistances due to polyhydramnios. Second, an increase in the resistance of chorionic veins due to polyhydramnios, assuming these veins act as Starling resistors. We then simulated the effects of polyhydramnios on different placental anastomotic patterns. The results were as follows. In the first mechanism (polyhydramnios affects AV-VA resistances), an increased amniotic fluid pressure hardly affected bidirectional AV, but slightly decreased fetofetal transfusion in AV plus AA anastomoses. However, for these effects to change the natural development of the pregnancy, polyhydramnios needed to persist for approximately 4 weeks, and by comparing the effects of polyhydramnios with the effects of amnioreduction, amnioreduction was more beneficial for normalizing the donor amniotic fluid volume. Therefore, these beneficial effects due to polyhydramnios have no practical clinical significance. In the second mechanism (Starling resistors for chorionic veins), polyhydramnios slightly increased fetofetal transfusion and hence slightly increased TTTS severity in bidirectional AV and AV plus VV, but did not affect AV plus AA anastomoses. In conclusion, we hypothesize that the simulated effects of polyhydramnios are not the primary cause that TTTS placentas include more often bidirectional AV than AV plus AA anastomoses. Rather, the more likely explanation is the previously identified larger range of AA than VA anastomotic diameters that adequately compensate for the effects of the AV.

Key words: polyhydramnios, monochorionic twin pregnancy, twin-twin transfusion syndrome, placental anastomoses, mathematical model, Starling resistor.

1. Introduction

Twin-twin transfusion syndrome (TTTS) is the pathological form of the circulatory imbalance that can develop between monochorionic twin fetuses. The syndrome is caused by one or more unidirectional arteriovenous (AV) placental connections between the twins, transfusing blood volume from the donor to the recipient at a rate that exceeds fetal growth of each twins' blood volume (van Gemert and Sterenborg 1998). Clinically, TTTS presents as severe oligohydramnios in one twin (the donor), which commonly becomes "stuck" in its membranes, and simultaneously polyhydramnios in the other twin (the recipient). Often, the twin pairs exhibit weight discordancy, with the donor demonstrating small for gestational age and the recipient being of normal size. More severe forms of TTTS may imply anemia and absent bladder filling in the donor twin, and polycythemia, hypertension, cardiac hypertrophy, tricuspid insufficiency and hydrops in the recipient (Quintero *et al* 1999).

The anatomy of the anastomoses is of importance to the pathophysiology of TTTS. First, AV anastomoses are connections at the capillary level located deep within the joint placental cotyledon, where arterial blood supply comes from a donor chorionic artery and venous drainage by a recipient chorionic vein. Often, however, AV fetofetal transfusion is compensated by oppositely directed (i.e., recipient to donor) transfusion from other anastomoses (Diehl *et al* 2001), which can be higher resistance (smaller size) opposite AV (denoted as VA), arterioarterial (AA) and venovenous (VV). Whereas AV and reverse VA are deep anastomoses, AA and VV anastomoses are direct superficial connections between chorionic arteries and veins, respectively, from both twins (Machin *et al* 2000). Although deep anastomoses may be a combination of AV and VA, the net fetofetal transfusion is by definition from donor to recipient, so ultimately in the AV direction. Conversely, due to the increased vascular pressures of the recipient, all superficial (i.e., AA and VV) fetofetal transfusions must occur from recipient to donor, although to some degree less than the net deep transfusion. Thus, compensating anastomoses may prevent or delay onset, or mitigate the severity of TTTS (van Gemert *et al* 2001a, Umur *et al* 2001a, Umur *et al* 2001b, Umur *et al* 2002).

TTTS is associated with significant mortality and neurological sequelae (van Gemert *et al* 2001a). Although there are numerous direct sequelae of anemia or polycythemia, the development of polyhydramnios may exacerbate the adverse outcomes. In singleton pregnancies, increased amniotic fluid pressure is inversely associated with fetal blood gas values (Fisk *et al* 1994). Polyhydramnios also increases uterine pressure and volume, often resulting in premature uterine contractions, preterm rupture of membranes and preterm labour and delivery. During the past decade, transabdominal amniotic fluid drainage (amnioreduction) of the polyhydramnios twin has become an accepted treatment for TTTS. Although amnioreduction seeks to reduce uterine volume and prolong the pregnancy, little is known of the impact of polyhydramnios on the fetoplacental circulation. In monochorionic twin placentae, polyhydramnios increases the placental vascular resistance, and amnioreduction significantly changes the pulsatility index of umbilical arteries (Zikulnig *et al* 1999). Polyhydramnios may thus also affect the degree of fetofetal transfusion and, hence, may reduce (van Gemert *et al* 2001b) or increase TTTS severity.

Recently, we developed a mathematical model of TTTS that predicts amniotic fluid volume and fetal growth related to the placental angioarchitecture (Umur *et al* 2001a). In this prior model, the effects of polyhydramnios on transplacental flow (fluid flow from mother to fetus) were assessed, although not the effects on net fetofetal transfusion. In the present study, we expanded our model to identify effects of increased amniotic fluid volume and pressure on the net fetofetal transfusion and, hence, on TTTS severity

2. Methods

2.1. Mathematical model

The mathematical model of twin amniotic fluid volumes and fetal blood volumes has been previously described (Umur *et al* 2001a). Briefly, input model parameters are the degree of placental sharing and the resistances of AV, VA, AA and VV anastomoses throughout gestation (van Gemert and Sterenborg 1998). The model includes 10 coupled differential equations, which assess interactions of fetal blood volume and osmolality, swallowing, urine production, and amniotic fluid volume and composition. Growth of fetal total body fluid, including fetal blood volume, and amniotic fluid volume is a result of transplacental fluid flow from maternal to fetal blood. Anastomotic fetofetal transfusions alter donor and recipient physiologic parameters throughout gestation. The stuck donor twin (i.e., amniotic fluid volume <10 ml) and polyhydramnios sequence of TTTS develops once the net fetofetal transfusion increases to a greater degree than the increase in fetal blood volume growth of each of the twins (van Gemert and Sterenborg 1998). Our model can simulate severe as well as mild forms of TTTS, where severity is related to the difference in hemodynamic capacity between compensating (i.e., VA, AA, VV) and primary AV anastomoses (Umur *et al* 2001a). Milder forms of TTTS either show spontaneous reaccumulation of donor amniotic fluid, or retain significant donor urine production, despite a persistent stuck donor twin (Umur *et al* 2001a).

In our original mathematical model (Umur *et al* 2001a), we considered only the primary effects of increased amniotic fluid pressure on transplacental fluid flow (*Trans*), which is considered as the main source of fetal and amniotic fluid growth. *Trans* is assumed to depend on a dynamic balance between the hydrostatic pressures and colloid osmotic pressures across the placenta

$$Trans = L_{pl}[(P_{mat} - (P_{amn} + P_{fet})) - (COP_{mat} - COP_{fet})] \quad (1)$$

where L_{pl} (ml/week/mmHg) is the net transplacental filtration coefficient, P_{mat} is the maternal mean arterial blood pressure in the intervillous space, P_{amn} is the transmitted amniotic fluid pressure and P_{fet} is the fetal capillary blood pressure. COP_{mat}, COP_{fet} are the colloid osmotic pressures of the maternal blood and fetal blood, respectively. Within the fetal body, the transmitted amniotic pressure adds equally to arterial and venous pressures, so it is added to the fetal capillary pressure. From Eq.1, therefore, an increased amniotic fluid pressure decreases the transplacental flow from mother to fetus.

The compliance of the uterus is defined as normal amniotic fluid volume divided by normal amniotic fluid pressure throughout gestation.

2.2. First mechanism: Increase in AV-VA resistances due to polyhydramnios

We have assumed and modeled the resistance increase in the placental capillaries and hence in the AV and VA anastomoses as a function of polyhydramnios severity. In this mechanism, we have assumed that capillary resistance remains normal until polyhydramnios develops, after which resistance increases linearly with the amount of excess amniotic fluid volume, proportional to the excess amniotic fluid pressure. We have defined polyhydramnios as at least twice the normal amniotic fluid volume (Umur *et al* 2001b). Since the relation between capillary AV and VA resistances and excess amniotic fluid volume is unknown, we have chosen several functions relating the two parameters (Fig.1).

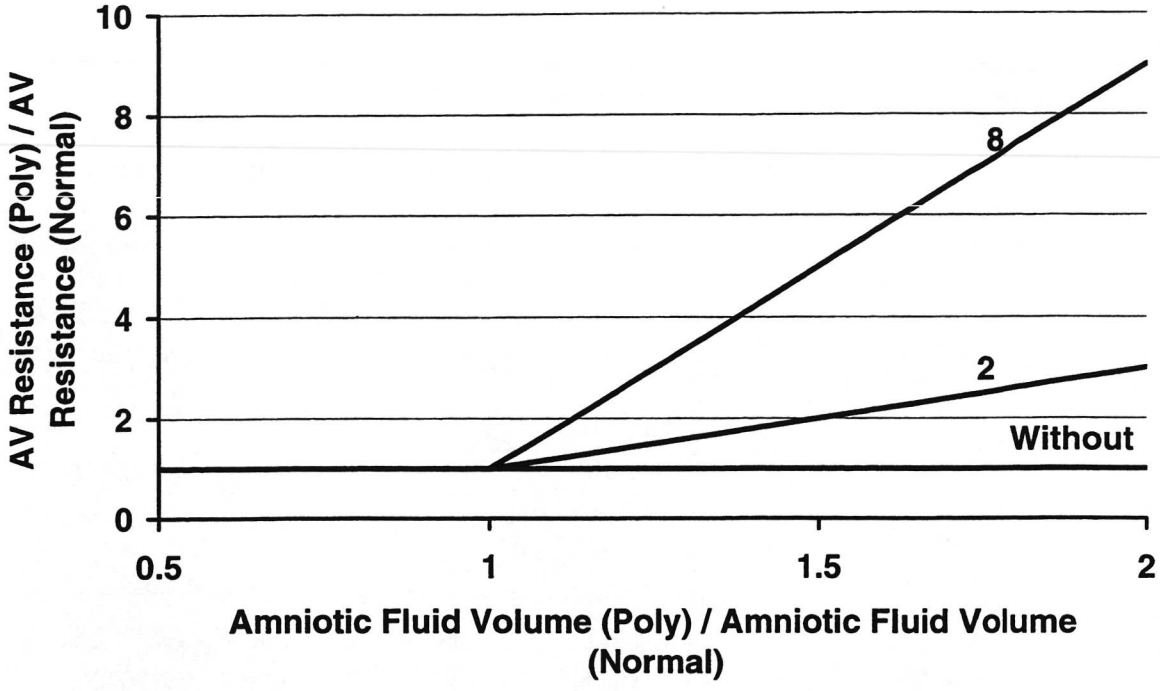

Fig.1 The ratio of AV anastomotic resistance with polyhydramnios to normal AV anastomotic resistance versus the ratio of polyhydramniotic to normal amniotic fluid volume for different slopes (**2, 8**). **Without:** AV resistance ratio without polyhydramnios.

In this first mechanism we only included the AV-VA resistance increase due to capillary compression by polyhydramnios, but not an increase in superficial AA, VV resistances. Furthermore, we only considered AA anastomoses in our analysis, since VV anastomoses behave similar to AA (van Gemert and Sterenborg 1998).

2.2.1. Presentation of TTTS manifestations

Our mathematical model (Umur *et al* 2001a) suggested two different possibilities in the presentation of TTTS manifestations. First (presentation A), a stuck donor twin and polyhydramnios in the recipient's sac occur virtually simultaneously. Second (presentation B), polyhydramnios in the recipient's sac occurs earlier than a stuck donor twin. These different presentations can develop with both VA and AA compensatory anastomoses and cause different changes in net fetofetal transfusion, as will be shown below (results section).

We have chosen four anastomotic patterns of a primary AV and either secondary VA or AA to simulate TTTS: *Case A1:* AV plus VA anastomoses and simultaneous polyhydramnios and stuck twin. *Case A2:* AV plus AA anastomoses and simultaneous polyhydramnios and stuck twin. *Case B1:* AV plus VA anastomoses and polyhydramnios occurs earlier than a stuck twin. *Case B2:* AV plus AA anastomoses and polyhydramnios occurs earlier than a stuck twin.

2.3. Second mechanism: Chorionic veins act as Starling resistors

We have hypothesized that chorionic veins act as Starling resistors if the amniotic fluid pressure increases. We have defined normal amniotic pressure to be 1 mmHg less than fetal venous pressure, as amniotic fluid pressure is measured to be 1-3 mmHg lower than the venous pressure (Weiner *et al* 1989). We simulated three anastomotic patterns for TTTS:

Case C1: AV plus VA anastomoses. *Case C2*: AV plus VV anastomoses. *Case C3*: AV plus AA anastomoses.

We have included AV plus VV patterns here since, if the Starling mechanism is included for chorionic veins, VV anastomoses do not behave similar to AA, because of the lower hydrostatic pressures, i.e., Eq.2 below.

Pressure-flow relationships in collapsible tubes can be described by a Starling resistor which is defined as "a collapsible tube surrounded by a fluid filled rigid container in which the pressure external to the tube exceeds the outflow pressure" (e.g., Milnor, 1982). There are three separate conditions of flow (Q) through small collapsible tubes. When surrounding pressure (P_s) exceeds the outflow pressure (P_o) at constant inflow pressure (P_i), Q is driven by pressure difference (P_i - P_s). When P_o is raised so that it exceeds P_s, at constant P_i, Q is proportional to (P_i - P_o). More formally,

$$Q = (P_i - P_s)/R \quad \text{if} \quad P_i > P_s > P_o \tag{2a}$$

$$Q = (P_i - P_o)/R \quad \text{if} \quad P_i > P_o > P_s \tag{2b}$$

$$Q = 0 \quad \text{if} \quad P_s > P_i > P_o \tag{2c}$$

Here, R is the resistance of the fully open tube. It has been shown that these pressure flow interactions exist in the fetal circulation of the sheep placenta (Bissonnette and Farrell 1973).

3. Results

3.1. First mechanism: Increase in AV-VA resistances due to polyhydramnios
We created the following anastomotic parameters that simulate mild TTTS cases.

3.1.1 Polyhydramnios and a stuck donor twin occur simultaneously, cases A1 and A2
Case A1: AV plus VA anastomoses: Without modeling the effects of polyhydramnios (Umur *et al* 2001a), a stuck donor twin occurs at 19.7 weeks gestation but the donor twin starts to reaccumulate amniotic fluid spontaneously at 26 weeks (Fig.2). The net fetofetal transfusion from donor to recipient decreases (Umur *et al* 2001a) once the donor twin becomes stuck (not shown). Including the effects of polyhydramnios (i.e., increased AV and VA resistances), the additional decrease in net fetofetal transfusion due to polyhydramnios was minimal (not shown), and consequently, amniotic fluid behaviour for both recipient and donor twins was minimally affected (Fig.2).

Case A2: AV plus AA anastomoses: Without modeling the effects of polyhydramnios, a stuck donor twin occurs at 18.6 weeks gestation but the donor twin starts to reaccumulate amniotic fluid spontaneously at 26 weeks (Fig.3a). The AV transfusion, and hence the net fetofetal transfusion from donor to recipient, decreases (Umur *et al* 2001a) once the donor twin becomes stuck (Fig.3b). The sudden change in net fetofetal transfusion at about 26 weeks (indicated by "*R*") is due to reaccumulation of donor amniotic fluid. Including the effects of polyhydramnios did not influence net fetofetal transfusion before onset of a stuck twin. Hence it did not prevent occurrence of a stuck donor twin at 18.6 weeks. Nevertheless, net fetofetal transfusion decreased significantly with increased AV resistance (Fig.3b), causing earlier reaccumulation of the donor amniotic fluid (Fig.3a, and compare the different "*R's*" in Fig.3b).

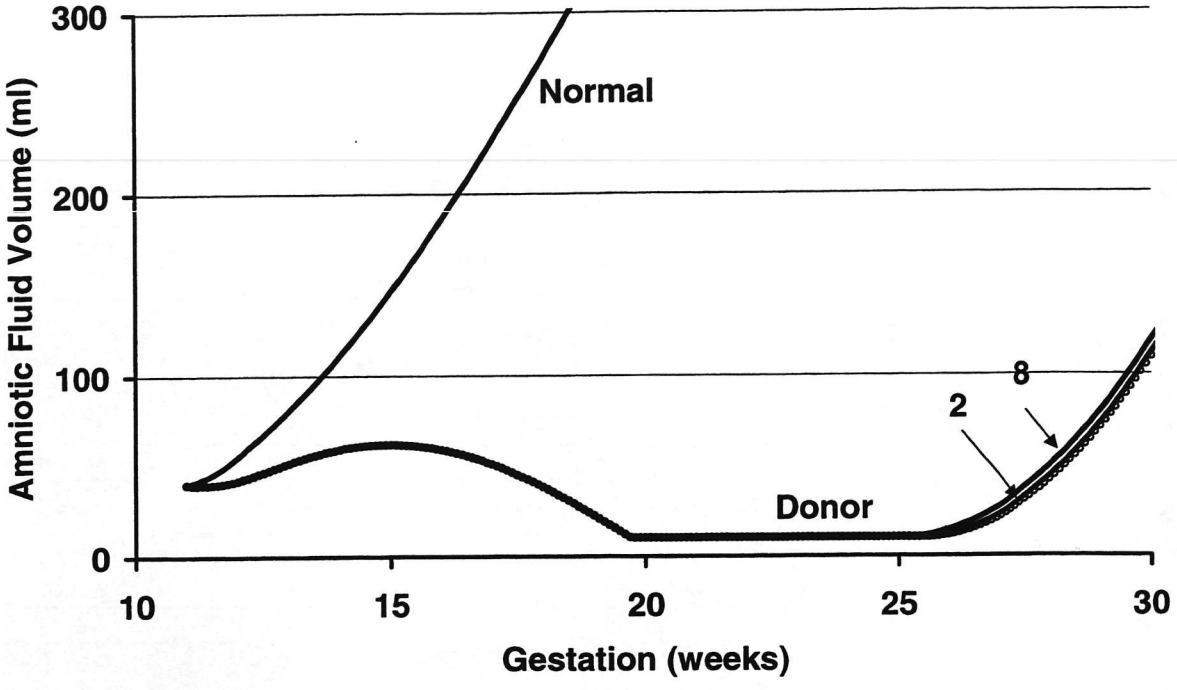

Fig.2 The results of donor's amniotic fluid volume versus gestation for the case of AV plus VA anastomoses (resistances at 40 weeks are 0.16 and 0.22 mmHg/ml/day respectively) with polyhydramnios and stuck twin occurring simultaneously (case A1). **Normal:** Normal amniotic fluid development. **Dotted line**: Without considering the effects of polyhydramnios. **2:** The slope of AV resistance increase is 2 (Fig.1), **8:** The slope of AV resistance increase is 8.

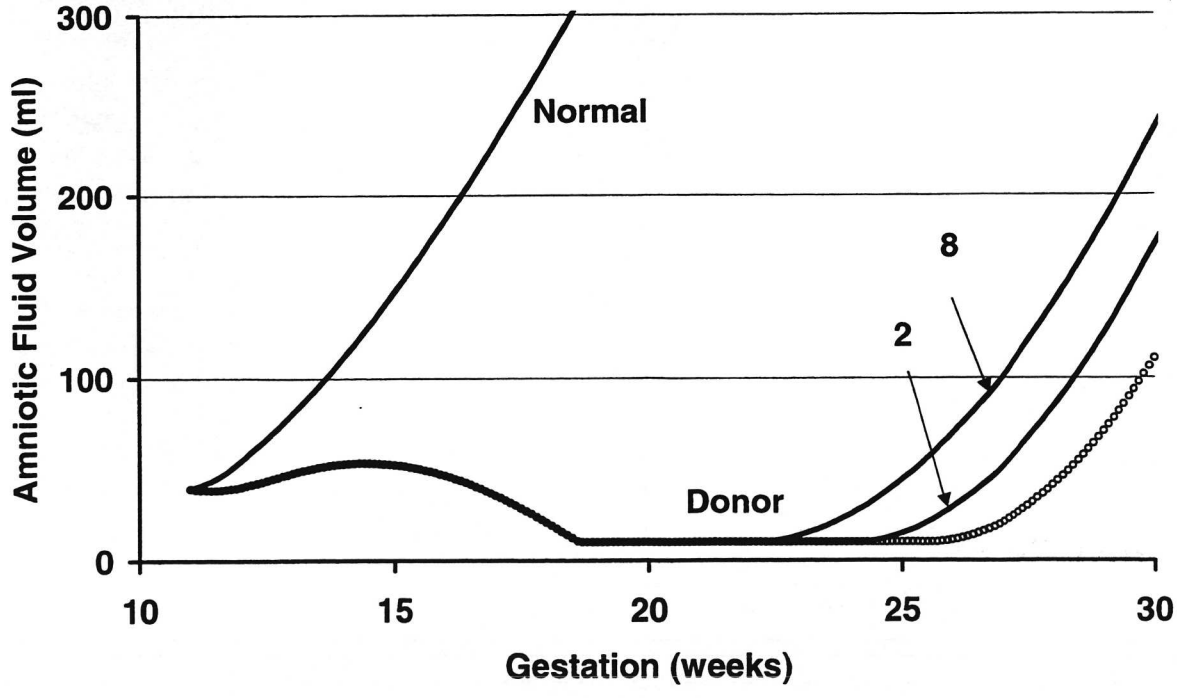

Fig.3a) The results of donor's amniotic fluid volume versus gestation for the case of AV plus AA anastomoses (resistances at 40 weeks are 0.43 and 0.16 mmHg/ml/day respectively) with polyhydramnios and stuck twin occurring simultaneously (case A2). **Normal:** Normal amniotic fluid development. **Dotted line**: Without considering the effects of polyhydramnios. **2:** The slope of AV resistance increase is 2 (Fig.1), **8:** The slope of AV resistance increase is 8.

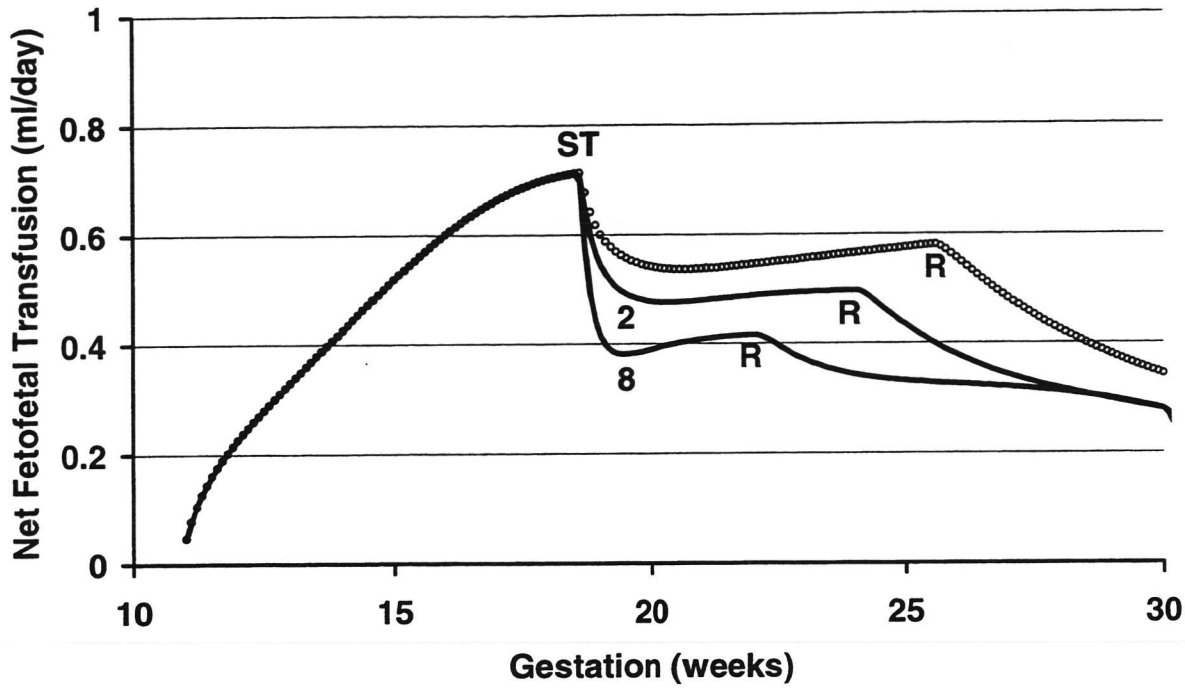

Fig.3b) The results of net fetofetal transfusion versus gestation for the case of AV plus AA anastomoses (resistances at 40 weeks are 0.43 and 0.16 mmHg/ml/day respectively) with polyhydramnios and stuck twin occurring simultaneously. **Dotted line**: Without considering the effects of polyhydramnios. **2:** The slope of AV resistance increase is 2 (Fig.1), **8:** The slope of AV resistance increase is 8. **ST:** stuck donor twin. **R:** reaccumulation of amniotic fluid volume in the donor.

3.1.2 Polyhydramnios occurs earlier than the stuck twin, cases B1 and B2

Case B1: AV plus VA anastomoses: Without modeling the effects of polyhydramnios, the donor twin becomes stuck at 23.5 weeks and remains stuck throughout pregnancy. Polyhydramnios begins earlier, at 21.5 weeks gestation. Including the effects of polyhydramnios (i.e., increased AV and VA resistances) causes a decrease in net fetofetal transfusion, which slightly delayed occurrence of a stuck donor twin, and spontaneous reaccumulation of the donor amniotic fluid (Fig.4).

Case B2: AV plus AA anastomoses: Without modeling the effects of polyhydramnios, the donor twin becomes stuck at 25.6 weeks and remains stuck throughout pregnancy, and polyhydramnios begins earlier, at 22.5 weeks gestation (Fig.5a). Including the effects of polyhydramnios, an increased AV resistance causes a decrease in the net fetofetal transfusion from donor to recipient (Fig.5b), and consequently prevented occurrence of a stuck donor twin (Fig.5). We emphasize however that polyhydramnios developed in the recipient at 22.5 weeks, albeit at reduced severity compared with neglecting polyhydramnios effects.

3.2. Second mechanism: chorionic veins act as Starling resistors

Case C1: AV plus VA anastomoses: We created a bidirectional AV anastomotic pattern that simulates a mild TTTS case. Without the Starling mechanism the donor twin just does not become stuck (Fig.6). With the Starling mechanism included, the donor twin becomes stuck at 27.3 weeks gestation. In our results polyhydramnios increases net fetofetal transfusion, hence, has an adverse effect on TTTS with bidirectional AV anastomoses.

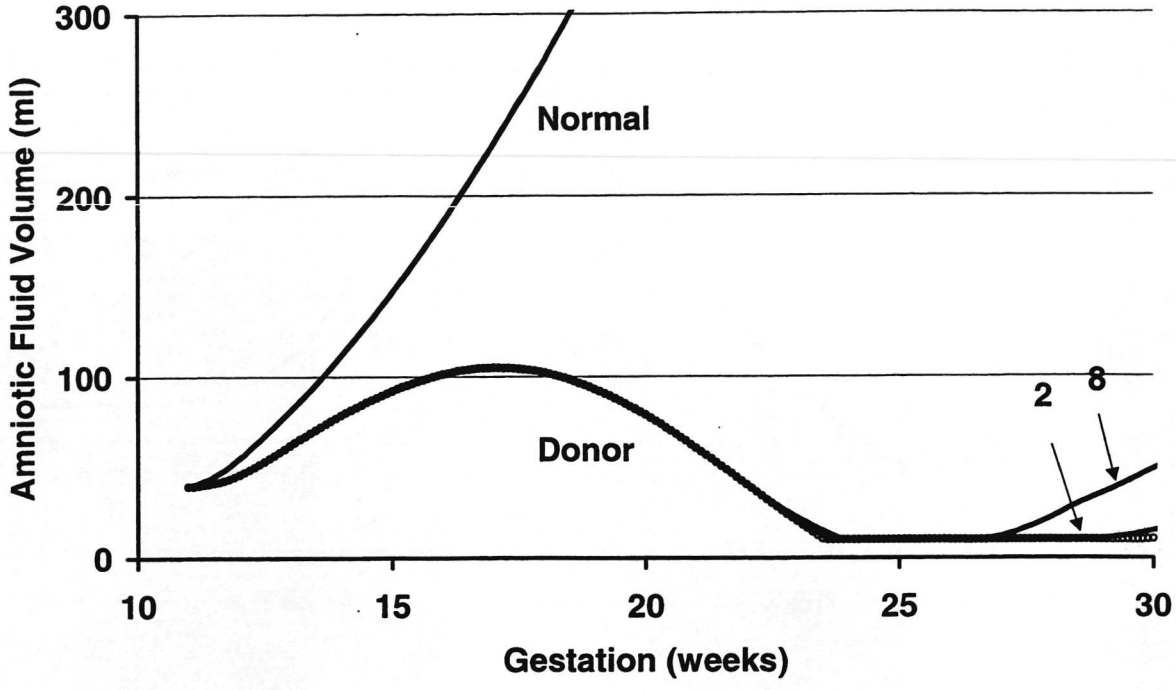

Fig.4 The results of donor's amniotic fluid volume versus gestation for the case of AV plus VA anastomoses (resistances at 40 weeks are 0.43 and 0.67 mmHg/ml/day respectively) with polyhydramnios occurring before a stuck twin (case B1). **Normal:** Normal amniotic fluid development. **Dotted line**: Without considering the effects of polyhydramnios. **2:** The slope of AV resistance increase is 2 (Fig.1), **8:** The slope of AV resistance increase is 8.

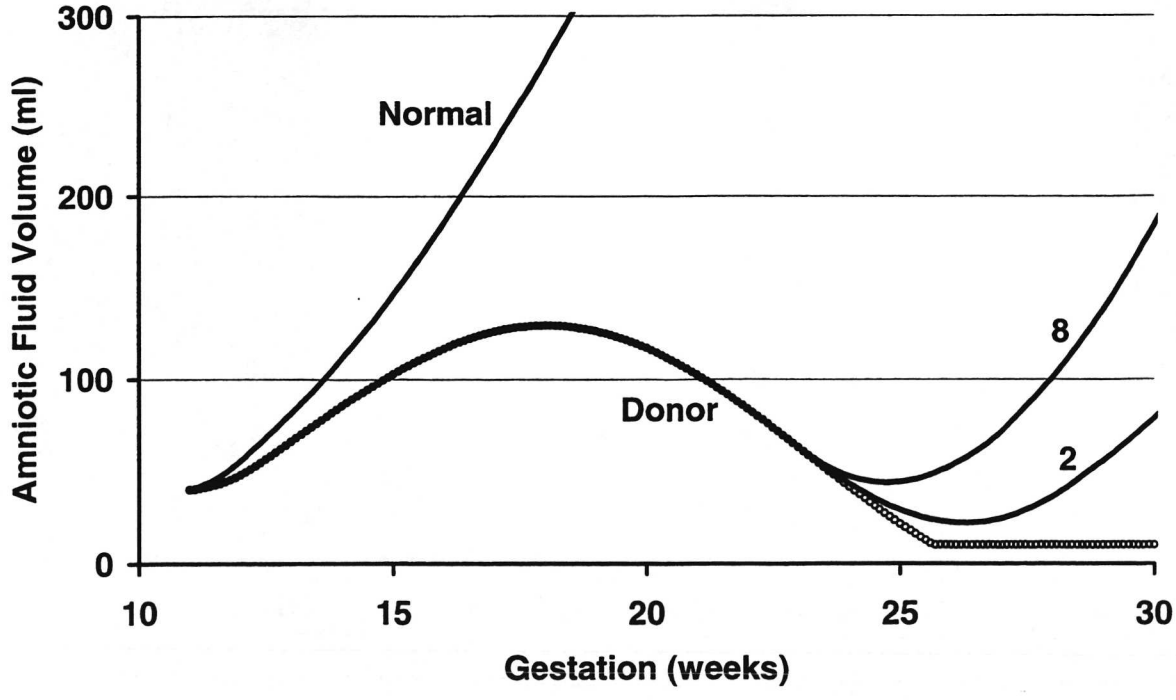

Fig.5a) The results of donor's amniotic fluid volume versus gestation for the case of AV plus AA anastomoses (resistances at 40 weeks are 1.66 and 0.95 mmHg/ml/day respectively) with polyhydramnios occurring before a stuck twin (case B2). **Normal:** Normal amniotic fluid development. **Dotted line**: Without considering the effects of polyhydramnios. **2:** The slope of AV resistance increase is 2 (Fig.1), **8:** The slope of AV resistance increase is 8.

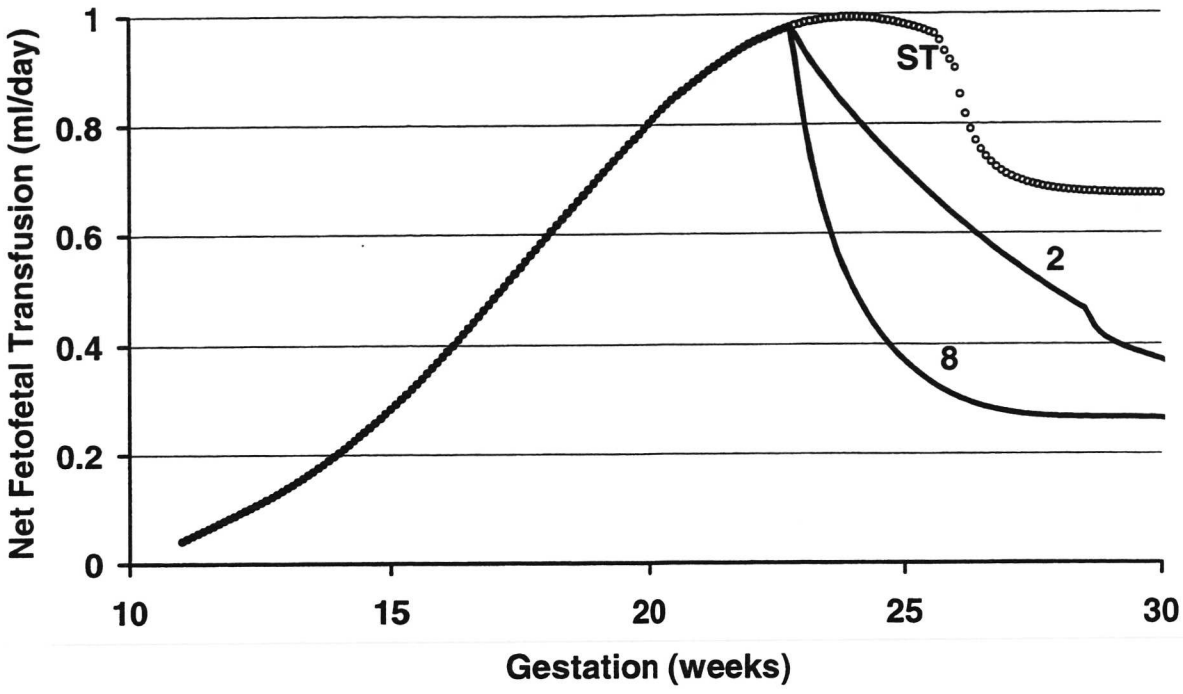

Fig.5b) The results of net fetofetal transfusion versus gestation for the case of AV plus AA anastomoses (resistances at 40 weeks are 1.66 and 0.95 mmHg/ml/day respectively) with polyhydramnios and stuck twin occurring simultaneously. **Dotted line**: The results of donor amniotic fluid volume versus gestation. **2:** The slope of resistance increase is 2 (Fig.1), **8:** The slope of resistance increase is 8. **ST:** stuck donor twin. **R:** reaccumulation of amniotic fluid volume in the donor.

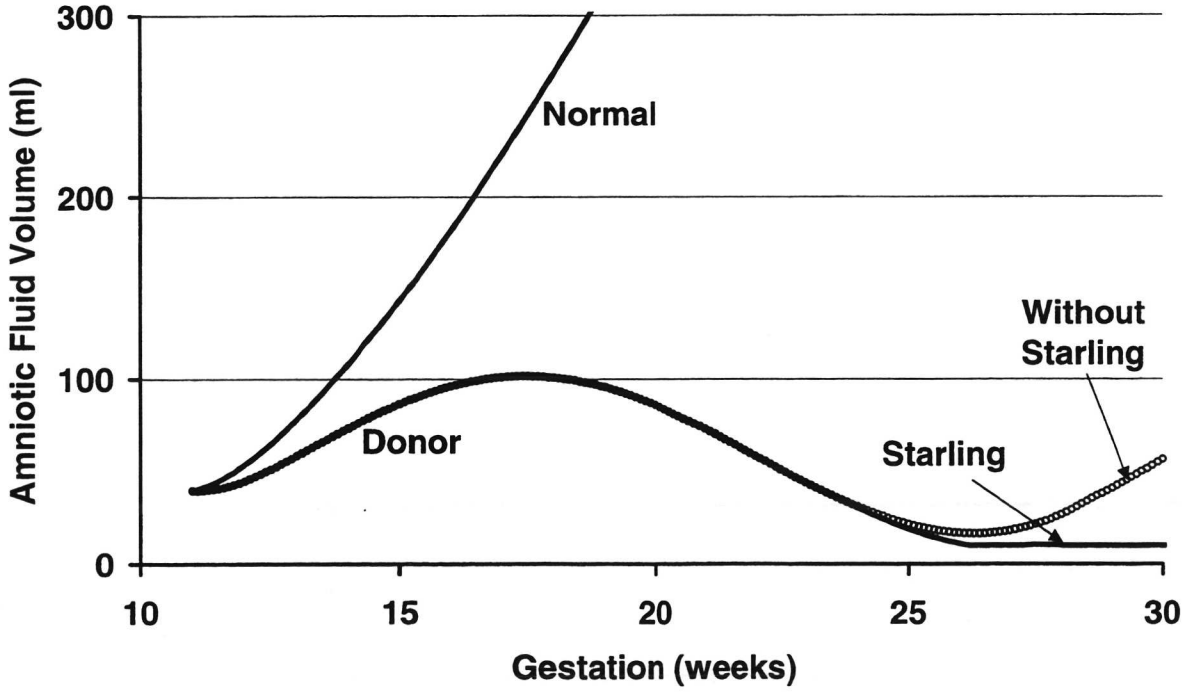

Fig.6 The results of donor amniotic fluid volume versus gestation with (**Starling**) and without (**without Starling**) applying Starling mechanism to the chorionic vessels for the case of AV plus VA anastomoses (resistances at 40 weeks are 0.33 and 0.49 mmHg/ml/day respectively) (case C1). **Normal:** Normal amniotic fluid development.

Case C2: AV plus VV anastomoses: Polyhydramnios also has an adverse effect on this case (results not shown). The mechanism is similar to the one described above. However, increased polyhydramnios severity could also completely occlude the VV anastomosis (if amniotic fluid pressure is higher than both donor and recipient venous pressures), leaving the AV uncompensated.

Case C3: AV plus AA anastomoses: Polyhydramnios did not have any effect on net fetofetal transfusion in this case (results not shown).

4. Discussion:

We have simulated two possible mechanisms to include the effects of an increased amniotic fluid pressure due to polyhydramnios on net fetofetal transfusion in monochorionic twin pregnancies.

4.1. First mechanism: increase in AV-VA resistances due to polyhydramnios

For TTTS presentation where a stuck donor occurs at the same time as polyhydramnios (cases A1 and A2), an increased amniotic fluid pressure had virtually no effect on net fetofetal transfusion of bidirectional AV anastomoses (case A1, Fig.2). For AV plus AA anastomoses (case A2), polyhydramnios reduced the net fetofetal transfusion, which obviously did not prevent occurrence of a stuck twin, but accelerated reaccumulation of donor amniotic fluid (Fig.3). For TTTS presentation where polyhydramnios develops earlier than a stuck donor twin (cases B1 and B2), polyhydramnios slightly reduced the net fetofetal transfusion before the donor becomes stuck in its membranes. This slightly delayed or prevented onset of a stuck donor twin and accelerated reaccumulation of donor amniotic fluid.

These results raise the question whether it may be clinically beneficial to maintain an increased amniotic fluid volume/pressure instead of performing amnioreduction. Therefore, we have simulated amnioreduction in cases where polyhydramnios was predicted to reduce the TTTS severity. Prevention of TTTS was only predicted in AV plus AA anastomotic pattern, when polyhydramnios develops before a stuck donor twin (Case B2). Here, we simulated an amnioreduction following onset of polyhydramnios in the recipient (at 22.5 weeks). Amnioreduction in this case was more favorable then maintaining polyhydramnios (Fig.7). Amnioreduction favors the transplacental fluid flow (from mother to fetus), which increases the blood volume of both fetuses (Umur *et al* 2001b). As a result, amnioreduction will increase the donor's urine production, hence, it will be beneficial for the donor fetus until polyhydramnios develops again. However, in the first mechanism, amnioreduction has an additional disadvantageous effect. Since polyhydramnios increased the AV anastomotic resistance, dissapearance of polyhydramnios with amnioreduction will decrease the AV resistance, hence will increase the net fetofetal transfusion. Nevertheless, in the example (Fig.7) the acute beneficial effects of the transplacental flow overcome the chronic negative effects of AV transfusion. Thus, amnioreduction is more beneficial than possible positive effects of polyhydramnios. Additionally, for polyhydramnios to delay or prevent a stuck donor twin it needed to persist for approximately 4 weeks (Figs. 3a and 4). Therefore, the beneficial effects of polyhydramnios have no practical clinical significance.

The increase in both AV and VA resistances due to polyhydramnios will decrease the AV and VA flows. Consequently, this mechanism decreases the net fetofetal transfusion from donor to recipient. However, this effect is not as strong as may be expected on this basis, because of the following opposing mechanism of hemodynamic adaptation. With the decreased AV flow due to AV resistance increase, the decrease in donor's arterial and venous pressures will slow down, and the increase in recipient's arterial and venous pressures will

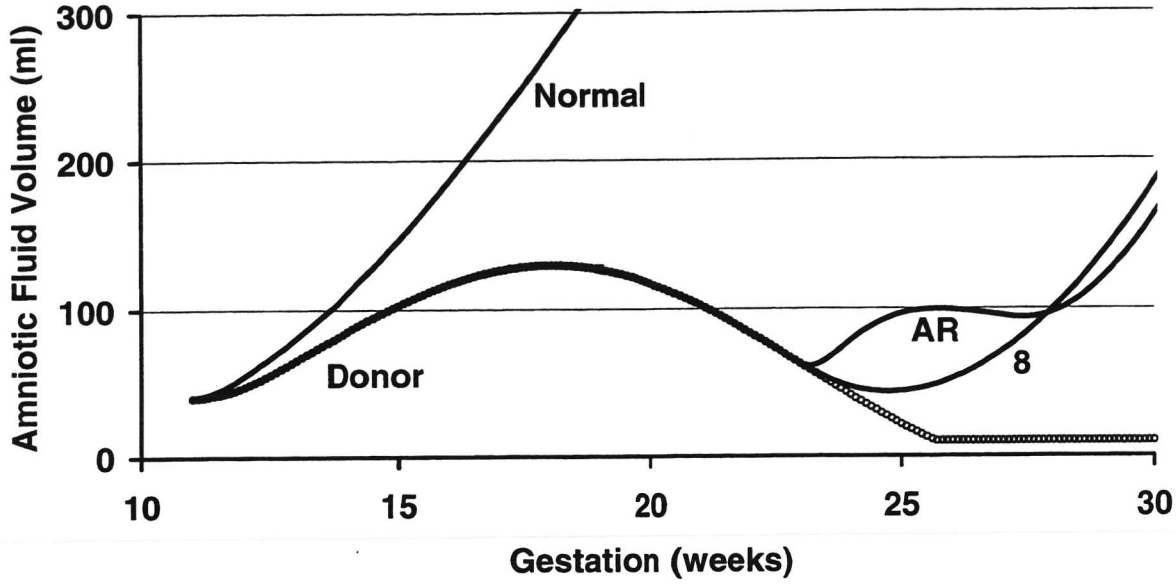

Fig.7 The results of donor amniotic fluid volume versus gestation for the case of AV plus AA anastomoses (resistances at 40 weeks are 1.66 and 0.95 mmHg/ml/day respectively) with polyhydramnios occurring before a stuck twin (case B2). **Normal:** Normal amniotic fluid development. **Dotted line**: Without considering the effects of polyhydramnios. **8:** The slope of AV resistance increase is 8 (Fig.1). Amnioreduction (**AR**) is done at 22.5 weeks of gestation. The amniotic fluid volumes removed was 541 ml.

also slow down. This opposing mechanism will therefore slightly increase the (decreasing) AV flow and decrease the VA flow. Thus, the net fetofetal transfusion from donor to recipient may not decrease as much as expected, based on the increase in AV-VA resistances only.

The increase in AV resistance due to polyhydramnios was previously touted to cause a decreased AV flow, but not directly a change in AA flow, so it would reverse the net fetofetal transfusion in AV plus AA patterns (van Gemert *et al* 2001b). However, because of the decreased AV flow, the donor arterial pressure will increase again, the recipient's arterial pressure will decrease, and consequently the AA flow will also decrease. A new hemodynamical equilibrium will be established (Figs. 3b and 5b). We emphasize that AA flow adjusts within hours, so virtually instantaneously, to changes in arterial blood pressures (van Gemert *et al* 1998).

To simulate this mechanism within our mathematical model (Umur *et al* 2001a), we increased the resistances of the AV and VA anastomoses linearly with the amount of excess amniotic fluid volume (Fig.1). Although the actual relations assumed in Fig.1 are unknown, we emphasize that our aim was to identify and understand the possible changes in net fetofetal transfusion and hence in hemodynamic and amniotic fluid behaviour in response to increased anastomotic AV and VA resistances due to polyhydramnios.

4.2. Second mechanism: chorionic veins act as Starling resistors.

Under the assumption that chorionic veins act as Starling resistors, the net fetofetal transfusion, hence, TTTS severity with bidirectional AV anastomoses is slightly adversely effected with polyhydramnios. When TTTS has developed, the donor twin's venous pressure

is smaller than the recipient's venous pressure. Increasing amniotic fluid pressure due to polyhydramnios will compress the donor chorionic veins first and therefore increases the VA resistance. Consequently, a decreased VA flow develops from recipient to donor, which will augment the effects of the AV flow from donor to recipient, causing increased TTTS severity. When the amniotic fluid pressure overcomes the recipient's venous pressure, the AV resistance increases so the AV flow starts to decrease. However, the overall effect of polyhydramnios on bidirectional AV anastomoses will be an increased net fetofetal transfusion from donor to recipient. In the case of AV plus VV anastomoses, polyhydramnios may occlude the VV anastomosis completely, leaving the AV uncompensated, resulting in increased TTTS severity.

4.3. Impact of polyhydramnios on the fetoplacental circulation

Although little is known of the impact of polyhydramnios on the fetoplacental circulation, we tacitly assumed in our original model (Umur *et al* 2001a) that an increased amniotic fluid pressure adds to the fetoplacental capillary pressure (Eqn.1). Since the transmitted amniotic pressure adds equally to arterial and venous pressures within the fetal body, the increased amniotic fluid pressure drives blood away from placenta to mother, rather than toward the fetus (Jauniaux *et al* 2001). Polyhydamnios also affects the placental resistance (Zikulnig *et al* 1999) and hence fetal development. Therefore, changes in fetal blood gas status (Fisk et al 1994) and redistribution of blood flow toward the brain (Scherjon *et al* 1993), likely are secondary effects of polyhydramnios.

Our assumption implies that amnioreduction increases the transplacental fluid flow from maternal to fetal circulations (Eqn.1), hence, drives fluid acutely toward donor and recipient fetuses. As a consequence, these fetuses may become stressed by this acute increase of their blood volume. If the recipient has already developed heart failure, or is close to developing this complication from volume overload, aggressive amnioreduction may be life threatening for this fetus.

In conclusion, we hypothesize that the simulated effects of polyhydramnios may not be the primary cause that TTTS placentas include more often bidirectional AV than AV plus AA anastomoses. Rather, the more likely explanation relates to the previously identified larger range of AA than VA anastomotic diameters that adequately compensate for the effects of the AV (Umur *et al* 2002).

REFERENCES

Bissonnette J M and Farrell R C 1973 Pressure-flow and pressure-volume relationships in the fetal placental circulation. *J Appl Physiol*, **35**, 355-360.

Diehl W, Hecher K, Zikulnig L, Vetter M and Hackelőer B-J 2001 Placental vascular anastomoses visualised during fetoscopic laser surgery in severe mid-trimester twin-twin transfusion syndrome. *Placenta*, in press.

Fisk N M, Vaughan J and Talbert D 1994 Impaired fetal blood gas status in polyhydramnios and its relation to raised amniotic pressure *Fetal Diagn Ther.* **9** 7-13.

Jauniaux E, Holmes A, Hyett J, Yates R and Rodeck C 2001 Rapid and radical amniodrainage in the treatment of severe twin-twin transfusion syndrome *Prenat Diagn*, **21**, 471-476.

Machin G A, Feldstein V A, van Gemert M J C, Keith L G and Hecher K 2000 Doppler sonographic demonstration of arterio-venous anastomosis in monochorionic twin gestation. *Ultrasound Obstet Gynecol*, **16**, 214-7.

Milnor W R 1982 *Hemodynamics*. Baltimore: Williams and Wilkins, pg 27.

Quintero R A, Morales W J, Allen M H, Bornick P W, Johnson P K and Kruger M 1999 Staging of twin-twin transfusion syndrome. *J Perinatol*, **19**, 550-5.

Scherjon S A, Smolders-De Haas H, Kok J H and Zondervan H A. 1993 The "brain-sparing" effec: antenatal cerebral Doppler findings in relation to neurologic outcome in very preterm infants *Am J Obstet Gynecol*, **169**, 169-175.

van Gemert M J C and Sterenborg H J C M 1998 Haemodynamic model of twin-twin transfusion syndrome in monochorionic twin pregnancies. *Placenta*, **19**, 195-208.

van Gemert M J C, Major A L and Scherjon S A 1998 Placental anatomy, fetal demise and therapeutic intervention in monochorionic twins and the transfusion syndrome: New hypotheses. *Eur J Obstet Gynecol Repr Biol*, **78**, 53-62.

van Gemert M J C, Umur A, Tijssen J G P and Ross M G 2001a Twin-twin transfusion syndrome: etiology, severity and rational management. *Curr Opin Obstet Gynecol*, **13**, 193-206.

van Gemert M J C, Kranenburg-Lakeman P, Milovanović Ž, Vergroesen I and Boer K 2001b Polyhydramnios and arterio-arterial placental anastomoses may beneficially affect monochorionic twin pregnancies. *Phys Med Biol*, **46**, N57-N63.

Umur A, van Gemert M J C and Ross M G 2001a Amniotic fluid and hemodynamic model in monochorionic twin pregnancies and twin-twin transfusion syndrome. *Am J Physiol Regulatory Integrative Comp Physiol*, **280**, R1499-R1509.

Umur A, van Gemert M J C and Ross M G 2001b Fetal urine and amniotic fluid in monochorionic twins with twin-twin transfusion syndrome: simulations of therapy. *Am J Obstet Gynecol*, **185**, 996-1003.

Umur A, van Gemert M J C, Nikkels P G J and Ross M G 2002 Monochorionic twins and twin-twin transfusion syndrome: the protective role of arterio-arterial anastomoses. *Placenta*, in press.

Weiner C P, Heilskov J, Pelzer G, Grant S, Wenstrom K and Williamson A R 1989 Normal valuse for human umbilical venous and amniotic fluid pressures and their alterations by fetal disease *Am J Obstet Gynecol* **161**, 714-7.

Zikulnig L, Hecher K, Bregenzer T, Bäz E and Hackelöer B J 1999 Prognostic factors in severe twin-twin transfusion syndrome treated by endoscopic laser surgery. *Ultrasound Obstet Gynecol.* **14**, 380-7.